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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,059	05/08/2007	James Kowalski	33554A	3254

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 101/2
EAST HANOVER, NJ 07936-1080

EXAMINER	
YU, HONG	
ART UNIT	PAPER NUMBER
1613	
MAIL DATE	DELIVERY MODE
12/06/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,059	KOWALSKI ET AL.	
	Examiner	Art Unit	
	HONG YU	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-80* is/are pending in the application.

4a) Of the above claim(s) *78-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/20/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments, arguments, and IDS filed 09/20/2010 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdraw. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application

Status of claims

Claims 1-55 have been canceled. Claims 56-80 are under examination in the instant office action.

Rejections withdrawn

Applicant's amendments have overcome the 112 (2nd paragraph) rejections from the previous Office Action.

Rejections remained

The following rejections of the claims are remained for reasons of record and the following.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 56-70, 75, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balkan et al. (WO 01/52825 A2).

Applicant's claims

The instant claims 56-63 and 77 recite a compressed or direct compressed tablet comprising (S)-1-[(3-hydroxy-1-adamantyl)amino]acetyl-2-cyano-pyrrolidine (LAF 237) particles with at least 60% of the particle size distribution is less than 250 μm, at least 80% of the particle size distribution is between 10 to 250 μm, and at least 25% or 35% of the particle size distribution is between 50 to 150 μm, tablet thickness to tablet weight ratios of 0.002 to 0.06 mm/mg and 0.001 to 0.03 mm/mg, water content of the tablet of less than 10% and less than 5% after 1 week at 25 ºC and 60% RH.

The instant claims 64-68 and 70 recite the said composition comprising 5-60%, 20-40%, 20-35, 22-28%, and 30-35% by weight of LAF 237; 40-95% , 62-78%, and 58-

72% by weight of diluent; 0-20%, 0-10%, and 1-6% by weight of disintegrant; 0.1-10% and 0.25-6% by weight of lubricant.

The instant claims 69 recite the composition comprising 25-70% by weight of microcrystalline cellulose as diluent or 25-70% by weight of microcrystalline cellulose with 5-40% by weight of lactose as diluent.

The instant claims 75 recite release profiles of the composition comprising LAF 237 particles with at least 60% of the particle size distribution is less than 250 μm as: between 0 and 10 minutes 85 to 99.5% of the active ingredient is released, and between 10 to 15 minutes 90 to 99.5% of the active of the active ingredient is released.

Determination of the Scope and Content of the Prior Art

(MPEP 2141.01)

Balkan et al. disclose a pharmaceutical composition comprising LAF 237 (page 6, line 10-12).

Balkan et al. disclose the composition comprising 20-60% of LAF 237 (page 30, line 17-29); 43.1% lactose and 21.9% microcrystalline cellulose as diluent (example 1); 5.7% croscarmellose sodium as disintegrant (example 1); 1.8% magnesium stearate as lubricant (example 1).

Ascertainment of the Difference between Scope of the Prior Art and the Claims

MPEP 2141.02)

Balkan et al. are silent about LAF 237 particles with at least 60% of the particle size distribution being less than 250 μm, at least 80% of the particle size distribution being between 10 to 250 μm, and at least 25% or 35% of the particle size distribution

being between 50 to 150 µm, tablet thickness to table weight ratios of 0.002 to 0.06 mm/mg and 0.001 to 0.03 mm/mg, water content of the tablet of less than 10% and less than 5% after 1 week at 25 ºC and 60% RH.

Balkan et al. are silent about the release profiles of the composition comprising LAF 237 particles with at least 60% of the particle size distribution being less than 250 µm as between 0 and 10 minutes 85 to 99.5% of the active ingredient is released and between 10 to 15 minutes 90 to 99.5% of the active of the active ingredient is released.

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP 2142-2143)

Particle size in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal particle size of LAF 237 in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of particle size of LAF 237 would have been obvious at the time of applicants' invention.

The tablet thickness to table weight ratio is clearly a design choice that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal tablet thickness to table weight ratios in order to best achieve the desired results, such as forming the tablets, swallowing the

tablets, handling the tablets by an elderly person, labeling the tablets, etc. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of tablet thickness to table weight ratio would have been obvious at the time of applicant's invention.

The water content of the tablet after 1 week at 25 ºC and 60% RH is affected by the particle size of the components. The smaller the particle size, the larger the surface area of the particle; therefore, the more absorption of moisture from the environment of the tablet comprising the particles. The absorption of moisture from the environment of the tablet can be adjusted by adjusting the particle size. The Balkan et al.'s composition comprises the same component (LAF 237) except the prior art is silent about the particle size which is routinely optimized by a person of ordinary skill in the art. It would have been obvious at the time of applicants' invention to optimization of particle size of LAF 237 to achieve "the water content of the tablet of less than 10% and less than 5% after 1 week at 25 ºC and 60% RH". Thus, absent some demonstration of unexpected results from the claimed parameters, it would have been obvious at the time of applicant's invention for a tablet comprising LAF 237 with optimized particle size to have "the water content of the tablet of less than 10% and less than 5% after 1 week at 25 ºC and 60% RH".

Concerning the claimed release profile of the tablet, it should be noted that the smaller the particle size, the faster the release of the active ingredient. The rate of releasing of active ingredient of the tablet can be adjusted by adjusting the particle size. The Balkan et al.'s composition comprising the same component (LAF 237) except the

prior art is silent about the particle size which is routinely optimized by a person of ordinary skill in the art. It would have been obvious at the time of applicants' invention to optimize the particle size of LAF 237 to achieve the desired release profiles. Thus, absent some demonstration of unexpected results from the claimed parameters, it would have been obvious at the time of applicant's invention for tablet comprising LAF 237 with optimized particle size to have the release profiles recited in the claims.

Response to Applicants' arguments:

Applicants argue that example 1 taught by Balkan et al. does not teach LAF 237 in free form or in acid addition as the active in the compressed tablet with at least 60% of the LAF 237 particle size distribution in the tablet being less than 250 μm.

However, this argument is not deemed persuasive. First of all, according to Balkan et al. the examples are for illustration purpose and not intended to limit the scope of the invention. Nateglinide in example 1 together with LAF 237 are both actives taught by Balkan et al. Balkan et al. use nateglinide in all three examples, but indicate that LAF 237 is the most preferred active, thus it is reasonable to assert the examples also apply to tablets with other actives such as the most preferred active: LAF 237. Secondly, according to the teachings in page 6 line 10-12 LAF 237 is the most preferred of formula I which are in free form or in acid addition salt form. Thirdly, it has been pointed out by the examiner that particle size in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize, absent some demonstration of unexpected results from the claimed parameters, this

optimization of particle size of LAF 237 would have been obvious at the time of applicants' invention.

Claims 71-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balkan et al. (WO 01/52825 A2) as applied to claims 56-70, 75, and 77 above, and further in view of Burgess et al. (US 2004/0186046 A1).

Applicant's claims

The instant claims 71-74 recite composition comprising about 22% to about 28% by weight of LAF 237; 35-50% , 35-55%, and about 45% to about 50% by weight of microcrystalline cellulose; 18-35% and about 20% to about 25% by weight of lactose; 1-4%, 1.5 -2.5%, and about 1.5% to about 2.5% of by weight of sodium starch glycolate as disintegrant; and 0.5-4% and about 0.1 to about 2% by weight of magnesium stearate.

Determination of the Scope and Content of the Prior Art

(MPEP 2141.01)

The teachings of Balkan et al. are discussed above and applied in the same manner.

Ascertainment of the Difference between Scope of the Prior Art and the Claims

MPEP 2141.02)

Balkan et al. do not specify sodium starch glycolate as disintegrant, but specify croscarmellose sodium as disintegrant.

This deficiency is cured by Burgess et al. who teach a pharmaceutical composition comprising DP IV inhibitors and sodium starch glycolate as disintegrant (paragraph 181 and claim 3).

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP 2142-2143)

It would have been prima facie obvious at the time of the invention to a person of ordinary skill in the art to combine the teachings in Balkan et al. and Burgess et al. to substitute croscarmellose sodium with sodium starch glycolate. Croscarmellose sodium and sodium starch glycolate are well known as disintegrants to a person of ordinary skill in the art at the time of the invention. It is generally considered to be prima facie obvious to substitute a disintegrant with another disintegrant which is taught by the prior art to be well known and useful for as disintegrant in order to form a composition that is to be used for an identical purpose. The motivation for substituting it flows from its having been used in Burgess et al., and from its being recognized in Burgess et al. as useful for the same purpose. As shown by the recited teachings, instant claims are no more than substituting conventional disintegrant.

Response to Applicants' arguments:

Applicants argue that Burgess et al. do not teach compressed pharmaceutical tablet containing particles comprising LAF 237.

However, this argument is not deemed persuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Burgess et al. reference is brought in to substitute one disintegrant (croscarmellose sodium taught by Balkan et al.) with another (sodium glycolate taught by Burgess et al.) in a tablet formulation comprising DPP IV.

Claim 76 is rejected under 35 U.S.C. 103(a) as being unpatentable over Balkan et al. (WO 01/52825 A2) as applied to claims 56- 75 and 77 above, and further in view of Koike (US 2004/0033258 A1).

Applicant's claims

The instant claim 76 recites a composition comprising LAF 237 particles with at least 60% of the particle size distribution is less than 250 µm and excipients with particle size distribution of between 5 and 400 µm.

Determination of the Scope and Content of the Prior Art

(MPEP 2141.01)

The teachings of Balkan et al. are discussed above and applied in the same manner.

Ascertainment of the Difference between Scope of the Prior Art and the Claims

MPEP 2141.02)

Balkan et al. are silent about particle size distribution of excipients as being between 5 and 400 µm.

This deficiency is cured by Koike who teaches a pharmaceutical composition comprising LAF 237 and excipients with the particle size of the excipients as no more than 500 µm.

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP 2142-2143)

It would have been prima facie obvious at the time of the invention to a person of ordinary skill in the art to combine the teachings in Balkan et al. and Koike to specify particle size distribution of excipients as being between 5 and 400 µm. The effect of particle size on the formation of compressed tablets is well known to a person of ordinary skill in the art at the time of the invention. It is generally considered to be prima facie obvious to specify particle size of excipients which is taught by Koike to be well known and useful for forming the compressed tablets. The motivation for specifying it flows from its having been used in Koike. As shown by the recited teachings, instant claims are no more than the specifying particle size of conventional pharmaceutical excipients.

Response to Applicants' arguments:

Applicants argue that Koike does not teach compressed pharmaceutical tablet containing particles comprising LAF 237 with at least 60% of the LAF 237 particle size distribution in the tablet being less than 250 µm.

However, this argument is not deemed persuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA

1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Koike reference is brought in to specify the particle size of excipient being no more than 500 μm in a tablet formulation comprising DPP IV.

Respectfully, applicants' arguments are not persuasive. The predictable and expected result remains predictable and expected. Accordingly, the claims remain rejected for at least these reasons and the reasons of record.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brain-Yong Kwon can be reached on 571-272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/H. Y./
Examiner, Art Unit 1613

/Ernst V Arnold/
Primary Examiner, Art Unit 1613